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(54) **ANTAGONIST ANTIBODIES DIRECTED AGAINST CALCITONIN GENE-RELATED PEPTIDE AND METHODS USING SAME**

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(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

5,116,964 A *	5/1992	Capon et al. ....	536/23.5
7,479,488 B2	1/2009	Mueller et al.	
8,007,794 B2	8/2011	Zeller et al.	
8,293,239 B2	10/2012	Poulsen et al.	
8,298,536 B2	10/2012	Poulsen et al.	
2004/0110170 A1 *	6/2004	Pisegna et al. ....	435/6
2005/0234054 A1	10/2005	Mueller et al.	
2006/0183700 A1	8/2006	Vater et al.	

2009/0220489 A1	9/2009	Zeller et al.
2011/0054150 A1	3/2011	Poulsen et al.
2011/0257371 A1	10/2011	Poulsen et al.
2012/0009192 A1	1/2012	Zeller et al.
2012/0225075 A1	9/2012	Pios et al.

**FOREIGN PATENT DOCUMENTS**

EP 0212432 A1	3/1987
EP 1031350 A1	8/2000
JP 08-268874 A	10/1996
WO WO 03/093472 A2	11/2003
WO WO 2004/003019 A2	1/2004
WO WO 03/093472 A3	3/2004
WO WO 2004/003019 A3	9/2004
WO WO 2005/009962 A1	2/2005
WO WO 2005/100360 A1	10/2005
WO WO 2006/077212 A1	7/2006
WO WO 2007/025212 A2	3/2007
WO WO 2007/054809 A2	5/2007
WO WO 2007/061676 A2	5/2007
WO WO 2007/076336 A1	7/2007
WO WO 2007/054809 A3	8/2007
WO WO 2007/025212 A3	12/2007
WO WO 2007/061676 A3	12/2007
WO WO 2008/011190 A1	1/2008

**OTHER PUBLICATIONS**

Frobert et al. (1999). Peptides. 20:275-284.\*

U.S. Appl. No. 13/621,981, filed Sep. 18, 2012, Poulsen et al.

U.S. Appl. No. 13/623,206, filed Sep. 20, 2012, Poulsen et al.

U.S. Appl. No. 13/835,394, filed Mar. 25, 2013, Zeller et al.

U.S. Appl. No. 13/892,121, filed May 10, 2013, Poulsen et al.

U.S. Appl. No. 13/892,130, filed May 10, 2013, Poulsen et al.

Adwanikar, et al. Spinal CGRP1 receptors contribute to supraspinally organized pain behavior and pain-related sensitization of amygdala neurons. Pain. Nov. 2007;132(1-2):53-66. Epub Mar. 1, 2007.

Ambalavanar, et al. Deep tissue inflammation upregulates neuropeptides and evokes nociceptive behaviors which are modulated by a neuropeptide antagonist. Pain. Jan. 2006;120(1-2):53-68. Epub Dec. 13, 2005.

ATCC website search for PTA-6866 deposit (p. 1; Oct. 22, 2010).

ATCC website search for PTA-6867 deposit (p. 1; Oct. 22, 10).

Aziz. Visceral hypersensitivity: fact or fiction. Gastroenterology. Aug. 2006;131(2):661-4.

Balint, et al. Antibody engineering by parsimonious mutagenesis. Gene. Dec. 27, 1993;137(1):109-18.

Bennett, et al. Alleviation of mechanical and thermal allodynia by CGRP(8-37) in a rodent model of chronic central pain. Pain. May 2000;86(1-2):163-75.

Brorson, et al. Mutational analysis of avidity and fine specificity of anti-levan antibodies. J Immunol. Dec. 15, 1999;163(12):6694-701.

Brummell, et al. Probing the combining site of an anti-carbohydrate antibody by saturation-mutagenesis: role of the heavy-chain CDR3 residues. Biochemistry. Feb. 2, 1993;32(4):1180-7.

(Continued)

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**ABSTRACT**

The invention features methods for preventing or treating CGRP associated disorders such as vasomotor symptoms, including headaches (e.g., migraine, cluster headache, and tension headache) and hot flushes, by administering an anti-CGRP antagonist antibody. Antagonist antibody G1 and antibodies derived from G1 directed to CGRP are also described.

**9 Claims, 16 Drawing Sheets**